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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/412,284	10/05/1999	GRAHAM P. ALLAWAY	43966-CA-PCT	9473

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JOHN P WHITE
COOPER AND DUNHAM LLP
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	24

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/412,284	ALLAWAY ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

Continued Prosecution Application

1. Acknowledgement is hereby made of receipt and entry of the amendment submitted 25 August, 2003, wherein claims 15-17 were amended. Claims 15-17 are the only pending claims in the instant application.

35 U.S.C. § 112, First Paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Amended claims 15-17 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). As previously set forth, in order to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had **possession** of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. **The issue raised in this application is whether the original application provides adequate support for the broadly claimed genus of antibodies that are capable of inhibiting the fusion of macrophage-tropic HIV-1 isolates, but not**

T cell-tropic isolates, to the appropriate cell targets. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). **The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest.** *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). **A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process.** See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). The court noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention

is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., **complete or partial structure,** other **physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure,** or some combination of such characteristics. For some biomolecules, examples of identifying characteristics include a **nucleotide or amino acid sequence, chemical structure, binding affinity, binding specificity, and molecular weight.** The written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. **Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely.** In the latter case, **disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement.** *Regents of the University of California v. Eli Lilly,* 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied,* 523 U.S. 1089 (1998). *In re Wilder,* 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

As previously set forth, the disclosure (see p. 60) describes the isolation and preparation of four hybridomas (designated PA-3, -5, -6, and -7) that secrete antibodies that are capable of inhibiting HeLa-env_{JR-FL} fusion to PM1 cells in an *in vitro* RET assay. However, **no detailed structural or functional**

characterizations of the monoclonal antibodies produced by these hybridomas was provided. No detailed structural characterization was performed pertaining to the antigenic determinants recognized by said hybridoma supernatants. Thus, the binding specificity and coding potential of the antibodies has not been clearly ascertained. The skilled artisan would reasonably conclude that applicants were in possession of the four aforementioned hybridomas. However, the binding specificity of these antibodies remains to be elucidated. Thus, it is not readily manifest if these antibodies have the claimed characteristics (e.g., inhibition of macrophage-tropic virus fusion without inhibiting T-cell-tropic isolates to the degree indicated). Since the disclosure fails to provide adequate guidance pertaining to the structure of the claimed antibodies, the structure of the recognized antigenic determinants, a reproducible method for making antibodies with the desired phenotype, and a reasonable nexus between antibody structure and the claimed functional activities, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed invention.

Response to Arguments

4. Applicants traverse and proffer several arguments. First, applicants contend that most of the case law relied upon does not directly support the Examiner's position. This argument is clearly not persuasive. The case law relied upon provides a clear overview of the written description requirements and the obligations that must be met by applicants concerning this section. While some of the case particulars may differ, nevertheless, the general principles guiding the written description requirement are directly applicable to the instant application as previously set forth in the preceding paragraph. Second, applicants provide a supplemental declaration by Dr. Paul J. Maddon (one of the named inventors)

arguing that applicants were in full possession of the claimed invention. Applicants also reference an earlier filed declaration by Dr. Maddon. The arguments and content of that declaration have already been addressed. Dr. Maddon argues in the supplemental declaration that the claimed antibodies can be produced irrespective of whether or not the skilled artisan has any knowledge regarding the structural characteristics of the antibody. It was further argued that the lack of structural information on the antigenic determinants and monoclonal antibody would not necessitate undue experimentation by the skilled artisan. These arguments are not deemed to be persuasive either. The claims are clearly directed toward monoclonal antibodies with particular fusion inhibitory properties. The disclosure clearly fails to identify the molecular antigenic determinants recognized by the claimed Mabs. Thus, the Mabs of interest may recognize the same or entirely different epitopes. Moreover, the epitopes may be conformation-dependent and only present during cell-fusion events, which would make their identification even more difficult. Finally, the disclosure clearly fails to provide any nexus between the structure of the antibody and the claimed functional characteristics. Which portions of the antibody are required for the desired activities? What is the binding specificity of the claimed antibodies? What are the molecular determinants modulating antigen-antibody binding? The disclosure is incapable of addressing any of these critical elements because the inventors have failed to adequately characterize the claimed antibodies and epitope(s) recognized.

It was additionally argued by declarant, that it is common for inventors to characterize antibodies simply in terms of their binding characteristics (e.g., see U.S. Patent Nos. 4,381,295 and 5,993,816). First, applicants are advised that the court recognizes that the issuance of "related" claims to another is immaterial to the patentability of the claims under examination.

Ex parte Balzarini, 21 U.S.P.Q.2d 1897 (USPTO Bd. Pat. App. Int., 1991). The court concluded that "it is well settled that whether similar claims have been allowed to others is immaterial." The court further emphasized that "Whether obvious claims have been allowed to other patent applicants is immaterial." *In re Giolito*, 530 F.2d 397, 188 U.S.P.Q. 645 (1976). The court also added that "We reject appellants' argument that the instant claims are allowable because similar claims have been allowed in a patent. It is immaterial whether similar claims have been allowed to others. See *In re Margaroli*, 50 C.C.P.A. 1400, 318 F.2d 348, 138 U.S.P.Q. 158 (1963); *In re Wright*, 45 C.C.P.A. 1005, 256 F.2d 583, 118 U.S.P.Q. 287 (1950); *In re Launder*, 41 C.C.P.A. 887, 212 F.2d 603, 1001 U.S.P.Q. 391 (1954)." Furthermore, section 1701 of the M.P.E.P. suggests that it is inappropriate for P.T.O. employees to discuss questions of validity or invalidity concerning issued patents with individuals outside the PTO.

5. Amended claims 15-17 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. As previously set forth the claims are broadly directed toward antibodies that are capable of inhibiting macrophage-tropic HIV-1 isolate fusion to a suitable target cell without inhibiting T-cell-tropic isolate fusion to a suitable target cell. The disclosure describes the isolation and preparation (see p. 60) of four hybridomas (designated PA-3, PA-5, PA-6, and PA-7) that secrete antibodies that are capable of inhibiting HeLa-env_{JR-FL} fusion to PM1 cells in an *in vitro* RET assay. However, the disclosure fails to provide detailed structural or functional characterizations of the monoclonal antibodies produced by these hybridomas was provided. No detailed

structural characterization was performed pertaining to the antigenic determinants recognized by said hybridoma supernatants. No detailed studies were performed providing a nexus between antibody structure and the recited fusion inhibitory activities. Thus, the binding specificity and coding potential of the antibodies has not been clearly ascertained. Nevertheless, despite these numerous shortcomings in the specification, appropriate amendment of the claim language to encompass those specific hybridomas described (e.g., PA-3, PA-5, PA-6, and PA-7) would be acceptable (i.e., An isolated and purified monoclonal antibody designated PA-3, wherein said antibody is produced from the hybridoma cell line XXXXX having the ATCC designation NNNNNN, and said antibody has the following binding characteristics and activities ...). Absent appropriate amendment of the claims, the rejection is proper and maintained.

The legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows: **1) The disclosure fails to provide adequate guidance pertaining to the structural requirements of any given antibody.** Antibodies are large and complex molecules comprised of two ~55 kDa heavy chain polypeptides and two ~25 kDa light chain polypeptides (Frazer and

Capra, 1999). Within each chain are relatively constant regions and highly variable regions. It is the highly variable regions of these molecules that dictate many of the functional properties of the antibody such as antigen binding specificity. However, it is well-known in the art that antibody structure is highly variable due to the genetic diversity of the antibody locus (Max, 1999). The recombinatorial events involved in antibody production can produce 32 million different combinations. Thus, the skilled artisan cannot predict what the structure of any given antibody will be.

2) The disclosure fails to provide any guidance pertaining to the structure of the antigenic determinants recognized by the antibodies of interest. Antibody-antigen binding interactions generally involve between five to eight amino acids. However, single amino acid changes the antigenic determinant can drastically reduce or completely abrogate antigen-antibody binding (Mateu *et al.*, 1992; Alexander *et al.*, 1992). Thus, in order to reproducibly generate antibodies with the desired characteristics, the skilled artisan would require a knowledge of the antigenic determinants modulating this interaction. However, the specification is silent pertaining to this point.

3) The disclosure fails to provide a reproducible method for making antibodies with the claimed specificity. As noted *supra* in points one and two, there is considerable unpredictability pertaining to the generation of antibodies with the desired properties and characteristics. While the specification provides a generic method for producing antibodies, it fails to provide any reproducible methodologies for obtaining antibodies with the desired characteristics.

4) The claims are broadly directed toward a large genus of antibodies without providing sufficient structural and functional support pertaining to the properties of said antibodies.

5) The disclosure fails to provide a sufficient number of working embodiments. While four hybridomas were generated, the precise structural and functional characteristics of these antibodies were never clearly set forth.

6) The prior art is unpredictable and fails to provide any guidance pertaining to those macrophage-tropic-specific immunogenic/antigenic determinants that can be used to produce antibodies with the desired binding specificity. As noted *supra* in points one and two, considerable unpredictability was present in the art at the time of filing. However, the disclosure fails to address any of these concerns.

7) Legal precedence dictates that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970). *In re Vaeck*, 20 U.S.P.Q.2d 1438 (C.A.F.C. 1991). *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). Thus, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Response to Arguments

6. Applicants traverse and again argue assert that it is not necessary for one of ordinary skill in the art to know the antigenic determinants required for immunization. Applicants again submit that an earlier filed declaration by Dr. Maddon, as well as, the supplemental declaration accompanying the amendment, provide sufficient support for the claimed invention. Dr. Maddon argues in the supplemental declaration that the claimed antibodies can be produced irrespective of whether or not the skilled artisan has any knowledge regarding the structural characteristics of the antibody. It was further argued that the lack of structural information on the antigenic determinants and monoclonal antibody would not

necessitate undue experimentation by the skilled artisan. These arguments are not deemed to be persuasive. The claims are clearly directed toward mononclonal antibodies with particular fusion inhibitory properties. The disclosure clearly fails to identify the molecular antigenic determinants recognized by the claimed Mabs. Thus, the Mabs of interest may recognize the same or entirely different epitopes. Moreover, the epitopes may be conformation-dependent and only present during cell-fusion events, which would make their identification even more difficult. Finally, the disclosure clearly fails to provide any nexus between the structure of the antibody and the claimed functional characteristics. Which portions of the antibody are required for the desired activities? What is the binding specificity of the claimed antibodies? What are the molecular determinants modulating antigen-antibody binding? The disclosure is incapable of addressing any of these critical elements because the inventors have failed to adequately characterize the claimed antibodies and epitope(s) recognized.

It was additionally argued by declarant, that it is common for inventors to characterize antibodies simply in terms of their binding characteristics (e.g., see U.S. Patent Nos. 4,381,295 and 5,993,816). First, applicants are advised that the court recognizes that the issuance of "related" claims to another is immaterial to the patentability of the claims under examination. *Ex parte Balzarini*, 21 U.S.P.Q.2d 1897 (USPTO Bd. Pat. App. Int., 1991). The court concluded that "it is well settled that whether similar claims have been allowed to others is immaterial." The court further emphasized that "Whether obvious claims have been allowed to other patent applicants is immaterial." *In re Giolito*, 530 F.2d 397, 188 U.S.P.Q. 645 (1976). The court also added that "We reject appellants' argument that the instant claims are allowable because similar claims have been allowed in a patent. It

is immaterial whether similar claims have been allowed to others. See *In re Margaroli*, 50 C.C.P.A. 1400, 318 F.2d 348, 138 U.S.P.Q. 158 (1963); *In re Wright*, 45 C.C.P.A. 1005, 256 F.2d 583, 118 U.S.P.Q. 287 (1950); *In re Launder*, 41 C.C.P.A. 887, 212 F.2d 603, 1001 U.S.P.Q. 391 (1954)." Furthermore, section 1701 of the M.P.E.P. suggests that it is inappropriate for P.T.O. employees to discuss questions of validity or invalidity concerning issued patents with individuals outside the PTO.

Applicants additionally argue that the earlier submitted declaration provided by Dr. Maddon was not properly considered. This argument is not deemed to be persuasive. As previously set forth, the declarant asserted that methods for preparing the antibodies of interest were available at the time of filing. The Examiner did not dispute the finding that generic methods of preparing and isolating monoclonal antibodies were available. The problem is that a reproducible method that produces antibodies with the specifically claimed characteristics was not provided. There is considerable uncertainty pertaining to the generation of antibodies as previously set forth. Since the disclosure fails to identify the immunogenic/antigenic determinant(s) of interest and the structure of any given antibody, the skilled artisan has been extended an undue invitation to further experimentation. Moreover, the claims are directed toward a specific chemical compound (e.g., antibody) with defined structure and binding characteristics. However, the disclosure fails to provide any guidance pertaining to these structural and functional considerations. The declaration provided by Dr. Maddon fails to address these specific caveats. It only discloses generic methods of preparation and fails to provide any further illumination pertaining to the immunogenic/antigenic determinants modulating the antigen/antibody binding interactions and fails to provide any guidance pertaining to the structure of any given antibody.

Finality of Office Action

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

8. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward the following Group 1600 fax number: (703) 872-9306. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, Laurie Scheiner or James Housel, can be reached at (703) 308-1122 or (703) 308-4027, respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

30 November, 2003

JAMES HOUSEL 12/1/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600